

THE ASSOCIATION BETWEEN THE VDR POLYMORPHISMS AND CARDIOVASCULAR DISEASES

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The vitamin D receptor (VDR), through the binding of 1,25 vitamin D and subsequently modulating the transcription of target genes, mediates the vitamin D endocrine system. It is involved in calcium homeostasis in a variety of tissues. In particular, calcified atherosclerotic plaques are much stiffer than non calcified lesions and biochemical data suggest that calcified areas are unlikely to be associated with sites of plaque rupture. It has recently been shown that the extent of vascular calcification was inversely correlated with 1,25 vitamin D levels. The association between the VDR polymorphisms and cardiovascular diseases has also been studied. Artaza et al. reported an association between BsmI genotype and blood pressure in healthy men, with higher levels of blood pressure in healthy men and women with the b allele. However, in Korean leadworkers, an opposite relationship has been reported. Ortlepp et al. reported an increase in susceptibility to calcific aortic valve stenosis in individuals with the B allele, but also a lack of relationship between the BsmI polymorphism and the severity of coronary artery disease. However, the same group has recently reported an increase in susceptibility to myocardial infarction associated to the presence of the B allele. These results are in harmony with those of Kammerer et al. reporting an association of the BB genotype with a higher intimal-medial thickness in carotid artery. Piorier et al. studied five polymorphisms of the VDR gene: BsmI, ApaI, TaqI, ATG/ACT at the translation initiation codon, and the fifth polymorphism in the 5' region: an A/G substitution at position -988 upstream from the first nucleotide of the promoter sequence. None of these polymorphisms, or haplotypes combining them, was associated with myocardial infarction. Pan et al. investigated the association between FokI and BsmI of the VDR gene polymorphisms and patients with coronary artery disease in a Chinese population. No significant differences were observed in the genotype and allele frequencies of the FokI and BsmI polymorphisms between the cases and controls. In summary, a vast amount of information has been collected through the years regarding the association of vitamin D polymorphisms with susceptibility to suffer cardiovascular diseases. It is also likely that differences in race, diet or even latitude could alter the influence of the polymorphisms on the susceptibility to diseases, diluting the effects observed in other populations. Furthermore, the lack of understanding of the cellular and molecular processes influenced by the polymorphisms makes the observational studies very difficult to interpret.